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Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: Golam Shameem Examiner # : _____ Date: 3/9/09

Art Unit: 1626 Phone Number: 2-0706 Serial Number: 10/588,169

Location (Bldg/Room#): 4A35 (Mailbox #): 5C18 Results Format Preferred (circle): PAPER DISK

MG

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Coupling reactions useful ---

Inventors (please provide full names): Christoph Krell

Hans Hint

Earliest Priority Date: 02/02/04

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

INVENTOR SEARCH

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=> fil capl; d que nos 130; fil casre; d que nos 141
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FILE COVERS 1907 - 12 Mar 2009  VOL 150 ISS 11
FILE LAST UPDATED: 11 Mar 2009  (20090311/ED)

Caplus now includes complete International Patent Classification (IPC)
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'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE


L6              STR
L8         61787 SEA FILE=REGISTRY SSS FUL L6
L9              STR
L11          300 SEA FILE=REGISTRY SUB=L8 SSS FUL L9
L12             STR
L17           10 SEA FILE=REGISTRY SUB=L8 SSS FUL L12
L18       300689 SEA FILE=REGISTRY SPE=ON  ABB=ON  16.525/RID AND 46.150.18/RID

L19        56716 SEA FILE=REGISTRY SPE=ON  ABB=ON  L8 AND L18 NOT L17
L20            7 SEA FILE=CAPLUS SPE=ON  ABB=ON  L17
L22          902 SEA FILE=CAPLUS SPE=ON  ABB=ON  L11
L23        15869 SEA FILE=CAPLUS SPE=ON  ABB=ON  L19
L27            1 SEA FILE=CAPLUS SPE=ON  ABB=ON  US2006-588169/AP
L28           12 SEA FILE=CAPLUS SPE=ON  ABB=ON  KRELL C?/AU
L29          165 SEA FILE=CAPLUS SPE=ON  ABB=ON  HIRT H?/AU
L30            2 SEA FILE=CAPLUS SPE=ON  ABB=ON  (L27 OR L28 OR L29) AND (L20
                 OR L22 OR L23)



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FILE CONTENT:1840 - 8 Mar 2009 VOL 150 ISS 11

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L6              STR
L8        61787 SEA FILE=REGISTRY SSS FUL L6
L35           2 SEA FILE=CASREACT SPE=ON  ABB=ON  KRELL C?/AU
L36           4 SEA FILE=CASREACT SPE=ON  ABB=ON  HIRT H?/AU
L40        3772 SEA FILE=CASREACT SPE=ON  ABB=ON  L8
L41           1 SEA FILE=CASREACT SPE=ON  ABB=ON  (L35 OR L36) AND L40


=> dup rem l41,l30
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PROCESSING COMPLETED FOR L41
PROCESSING COMPLETED FOR L30
L45           2 DUP REM L41 L30 (1 DUPLICATE REMOVED)
                ANSWER '1' FROM FILE CASREACT
                ANSWER '2' FROM FILE CAPLUS

=> d ibib abs hit 1; d ibib abs hitstr 2


L45  ANSWER 1 OF 2  CASREACT  COPYRIGHT 2009 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         143:229864  CASREACT  Full-text
TITLE:                    A preparation of (1H-tetrazol-5-yl)-biphenyl
                          derivatives, useful as intermediates for the
                          manufacture of angiotensin II receptor antagonists
INVENTOR(S):              Krell, Christoph; Hirt, Hans
PATENT ASSIGNEE(S):       Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE:                   PCT Int. Appl., 40 pp.
                          CODEN: PIXXD2
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DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005075462	A1	20050818	WO 2005-EP978	20050201
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005211500	A1	20050818	AU 2005-211500	20050201
CA 2553246	A1	20050818	CA 2005-2553246	20050201
EP 1716140	A1	20061102	EP 2005-707117	20050201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS				
CN 1914197	A	20070214	CN 2005-80003794	20050201
BR 2005007352	A	20070703	BR 2005-7352	20050201
JP 2007519684	T	20070719	JP 2006-550140	20050201
MX 2006008678	A	20061009	MX 2006-8678	20060801
KR 2006128993	A	20061214	KR 2006-715580	20060801
IN 2006CN02815	A	20070608	IN 2006-CN2815	20060801
US 20070129413	A1	20070607	US 2006-588169	20060802
NO 2006003920	A	20061030	NO 2006-3920	20060901
PRIORITY APPLN. INFO.:			GB 2004-2262	20040202
			WO 2005-EP978	20050201

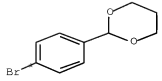
OTHER SOURCE(S): MARPAT 143:229864
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

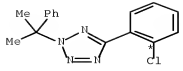
AB The invention relates to a preparation of (1H-tetrazol-5-yl)-biphenyl derivs. of formula I [wherein: Y is a tetrazole protecting group; R1 and R2 are independently alkyl or combined together form alkylene], useful as intermediates for the manufacture of angiotensin II receptor antagonists (no data). For instance, (1H-tetrazol-5-yl)-biphenyl derivative II was prepared via NiCl2(dppp)-catalyzed coupling of 4-([1,3]dioxan-2-yl)phenylmagnesium bromide with (chlorophenyl)tetrazole derivative III.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 13 A + B ===> C



A



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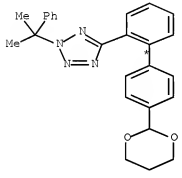


C

RX(1) RCT A 61568-51-2

STAGE(1)
RGT D 7439-95-4 Mg
SOL 109-99-9 THF
CON room temperature -> 50 deg C

STAGE(2)
CAT 106-93-4 BrCH2CH2Br
CON SUBSTAGE(1) 50 deg C
SUBSTAGE(2) 50 deg C -> reflux
SUBSTAGE(3) 40 minutes, reflux
SUBSTAGE(4) 1 hour, 60 deg C
SUBSTAGE(5) 60 deg C -> room temperature

STAGE(3)
CAT 15629-92-2 Ni complex
SOL 1634-04-4 t-BuOMe
CON room temperature -> 0 deg C

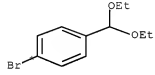
STAGE(4)
RCT B 179089-03-3
RGT E 7646-85-7 ZnCl2
SOL 109-99-9 THF, 1634-04-4 t-BuOMe
CON 0 deg C

STAGE(5)
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 20 hours, 0 deg C -> room temperature
SUBSTAGE(3) room temperature -> 0 deg C

STAGE(6)
RGT F 12125-02-9 NH4Cl
SOL 7732-18-5 Water

PRO C 862802-00-4
NTE Grignard reaction first two stages, Grignard reagent from stage two added to reaction mixture from stage four in stage five

RX(2) OF 13 L + M ===> N...



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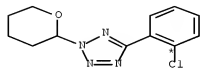

M

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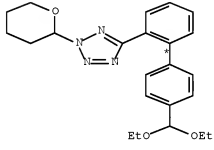


N

RX(2) RCT L 34421-94-6

STAGE(1)
RGT D 7439-95-4 Mg
SOL 109-99-9 THF
CON room temperature -> 40 deg C

STAGE(2)
CAT 106-93-4 BrCH2CH2Br
CON SUBSTAGE(1) 1 hour, 40 deg C
SUBSTAGE(2) 2 hours, 40 deg C
SUBSTAGE(3) 30 minutes, room temperature

STAGE(3)
CAT 15629-92-2 Ni complex
SOL 1634-04-4 t-BuOMe
CON room temperature -> 0 deg C

STAGE(4)
RCT M 676130-00-0
RGT E 7646-85-7 ZnCl2

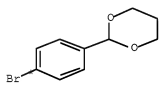
SOL 109-99-9 THF, 1634-04-4 t-BuOMe
CON 0 deg C

STAGE(5)
SOL 109-99-9 THF
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 5 hours, 0 deg C
SUBSTAGE(3) 19 hours, 0 deg C -> room temperature
SUBSTAGE(4) room temperature -> 0 deg C

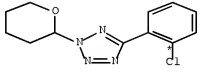
STAGE(6)
RGT F 12125-02-9 NH4Cl
SOL 7732-18-5 Water

PRO N 676130-06-6
NTE Grignard reaction first two stages, Grignard reagent from stage two added to reaction mixture from stage four in stage five, additional reactant isomer also present, alternate preparation also described

RX(3) OF 13 2 A + M + O ===> P + Q



2 A



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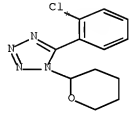

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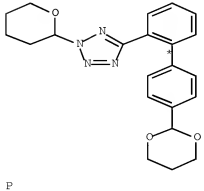

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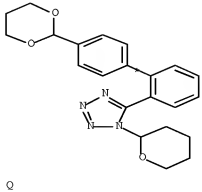


Q

RX(3)

STAGE(1)
RGT D 7439-95-4 Mg
SOL 109-99-9 THF
CON room temperature -> 10 deg C

STAGE(2)
RCT A 61568-51-2
CAT 106-93-4 BrCH2CH2Br
SOL 109-99-9 THF
CON SUBSTAGE(1) 10 deg C
SUBSTAGE(2) 90 minutes, 10 deg C
SUBSTAGE(3) 2 hours, 16 deg C
SUBSTAGE(4) 75 minutes, 25 deg C

STAGE(3)
CAT 15629-92-2 Ni complex
SOL 110-71-4 (CH2OMe)2
CON room temperature -> 0 deg C

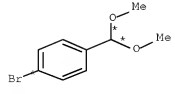
STAGE(4)
RCT M 676130-00-0, O 676130-01-1
RGT E 7646-85-7 ZnCl2
SOL 109-99-9 THF, 110-71-4 (CH2OMe)2
CON 0 deg C

STAGE(5)
CON SUBSTAGE(1) 1 hour, 0 deg C
SUBSTAGE(2) 3 hours, 0 deg C -> room temperature
SUBSTAGE(3) room temperature -> 0 deg C

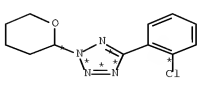
STAGE(6)
RGT F 12125-02-9 NH4Cl
SOL 7732-18-5 Water

PRO P 862802-02-6, Q 862802-03-7
NTE Grignard reaction first two stages, Grignard reagent from stage two added to reaction mixture from stage four in stage five, N2 isomer is the major product

RX(4) OF 13 2 S + M + O ===> 2
T



2 S



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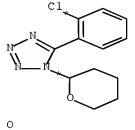

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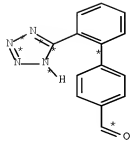

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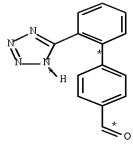


T

RX(4)

STAGE(1)
RGT D 7439-95-4 Mg
SOL 109-99-9 THF
CON room temperature -> 14 deg C

STAGE(2)
RGT U 1191-15-7 AlH(Bu-i)2
SOL 109-99-9 THF
CON 20 minutes, 14 deg C

STAGE(3)
RCT S 24856-58-4
SOL 109-99-9 THF
CON SUBSTAGE(1) 14 deg C
SUBSTAGE(2) 45 minutes, 14 deg C
SUBSTAGE(3) 2.5 hours, 25 deg C

STAGE(4)
RCT M 676130-00-0, O 676130-01-1
RGT E 7646-85-7 ZnCl2
CAT 15629-92-2 Ni complex
SOL 109-99-9 THF
CON room temperature -> 14 deg C

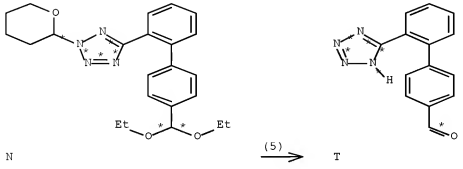
STAGE(5)
CON SUBSTAGE(1) 1 hour, <25 deg C
SUBSTAGE(2) 17.5 hours, room temperature

STAGE(6)
RGT V 7664-93-9 H2SO4
SOL 7732-18-5 Water, 64-17-5 EtOH
CON SUBSTAGE(1) 10 minutes, 50 deg C
SUBSTAGE(2) 50 minutes, 50 deg C
SUBSTAGE(3) 1.5 hours, 60 deg C
SUBSTAGE(4) overnight, 35 deg C

STAGE(7)
RGT W 7440-44-0 Carbon
CON 40 minutes, 60 deg C

PRO T 151052-40-3
NTE Grignard reaction first three stages, Grignard reagent from stage three added to reaction mixture from stage four in stage five, alternate preparations also described

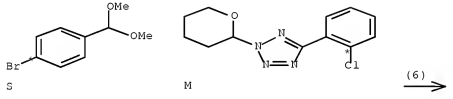
RX(5) OF 13 ...N ===> T



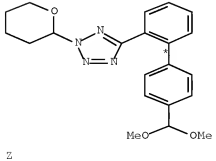
N T

RX(5) RCT N 676130-06-6
RGT Y 7647-01-0 HCl
PRO T 151052-40-3
SOL 7732-18-5 Water, 64-17-5 EtOH
CON 3 hours, room temperature -> 45 deg C
NTE alternate preparations also described

RX(6) OF 13 S + M ===> Z



S M



Z

RX(6)

STAGE(1)
RGT D 7439-95-4 Mg
SOL 109-99-9 THF
CON room temperature -> 14 deg C

STAGE(2)
RGT U 1191-15-7 AlH(Bu-i)2
SOL 109-99-9 THF
CON 20 minutes, 14 deg C

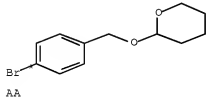
STAGE(3)
RCT S 24856-58-4
CON SUBSTAGE(1) 14 deg C
SUBSTAGE(2) 50 minutes, 14 deg C
SUBSTAGE(3) 2.5 hours, 25 deg C

STAGE(4)
RCT M 676130-00-0
CAT 15629-92-2 Ni complex
SOL 109-99-9 THF
CON room temperature -> 15 deg C

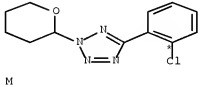
STAGE(5)
CON SUBSTAGE(1) 1 hour, <25 deg C
SUBSTAGE(2) 22.5 hours, room temperature

PRO Z 962802-04-8
NTE Grignard reaction first three stages, Grignard reagent from stage three added to reaction mixture from stage four in stage five, additional reactant isomer also present

RX(7) OF 13 AA + M ===> AB...



AA



M

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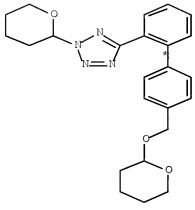


AB

RX(7)

STAGE(1)
RGT D 7439-95-4 Mg
SOL 109-99-9 THF
CON room temperature -> 14 deg C

STAGE(2)
RGT U 1191-15-7 AlH(Bu-i)2
SOL 108-88-3 PhMe
CON 20 minutes, 14 deg C

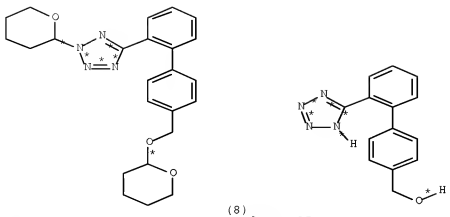
STAGE(3)
RCT AA 17100-68-4
CON SUBSTAGE(1) 14 deg C
SUBSTAGE(2) 40 minutes, 14 deg C
SUBSTAGE(3) 2.5 hours, 25 deg C

STAGE(4)
RCT M 676130-00-0
RGT E 7646-85-7 ZnCl2
CAT 15629-92-2 Ni complex
SOL 109-99-9 THF
CON room temperature -> 15 deg C

STAGE(5)
CON SUBSTAGE(1) 1 hour, <25 deg C
SUBSTAGE(2) 17.5 hours, room temperature

PRO AB 662802-05-9
NTE Grignard reaction first three stages, Grignard reagent from stage three added to reaction mixture from stage four in stage five, additional reactant isomer also present

RX(8) OF 13 ...AB ===> AD...



RX(8) RCT AB 862802-05-9

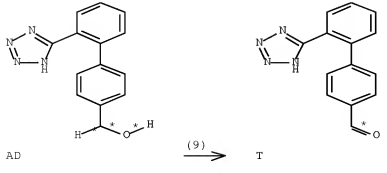
STAGE(1)
RGT V 7664-93-9 H2SO4
SOL 7732-18-5 Water, 64-17-5 EtOH
CON 3.5 hours, room temperature -> 45 deg C

STAGE(2)
SOL 7732-18-5 Water
CON SUBSTAGE(1) 45 deg C
SUBSTAGE(2) 45 deg C -> room temperature

STAGE(3)
RGT AE 1310-73-2 NaOH
SOL 7732-18-5 Water
CON room temperature, pH 2 - 3

PRO AD 160514-13-6

RX(9) OF 13 ...AD ===> T



RX(9) RCT AD 160514-13-6

STAGE(1)
RGT AF 67-68-5 DMSO, AG 121-44-8 Et3N
CON room temperature -> 12 deg C

STAGE(2)
RGT AH 28322-92-1 Pyridine-SO3
SOL 67-68-5 DMSO
CON 10 minutes, 12 deg C

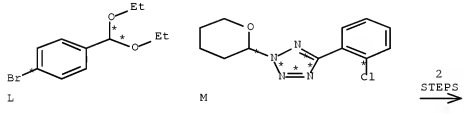
STAGE(3)
RGT AG 121-44-8 Et3N
CON <48 hours, room temperature

STAGE(4)
SOL 141-78-6 AcOEt
CON room temperature -> 5 deg C

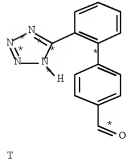
STAGE(5)
RGT Y 7647-01-0 HCl
SOL 7732-18-5 Water

PRO T 151052-40-3
NTE alternate preparations also described

RX(10) OF 13 COMPOSED OF RX(2), RX(5)
RX(10) L + M ===> T



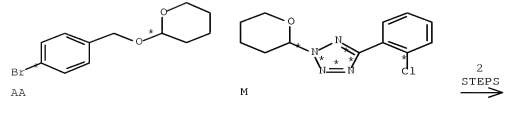
L M

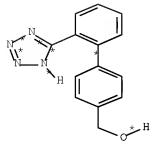


T

RX(2) RCT L 34421-94-8

```
            STAGE(1)
               RGT  D 7439-95-4 Mg
               SOL  109-99-9 THF
               CON  room temperature -> 40 deg C

            STAGE(2)
               CAT  106-93-4 BrCH2CH2Br
               CON  SUBSTAGE(1) 1 hour, 40 deg C
                    SUBSTAGE(2) 2 hours, 40 deg C
                    SUBSTAGE(3) 30 minutes, room temperature

            STAGE(3)
               CAT  15629-92-2 Ni complex
               SOL  1634-04-4 t-BuOMe
               CON  room temperature -> 0 deg C

            STAGE(4)
               RCT  M 676130-00-0
               RGT  E 7646-85-7 ZnCl2
               SOL  109-99-9 THF, 1634-04-4 t-BuOMe
               CON  0 deg C

            STAGE(5)
               SOL  109-99-9 THF
               CON  SUBSTAGE(1) 1 hour, 0 deg C
                    SUBSTAGE(2) 5 hours, 0 deg C
                    SUBSTAGE(3) 19 hours, 0 deg C -> room temperature
                    SUBSTAGE(4) room temperature -> 0 deg C

            STAGE(6)
               RGT  F 12125-02-9 NH4Cl
               SOL  7732-18-5 Water

         PRO  N 676130-06-6
         NTE  Grignard reaction first two stages, Grignard reagent from stage
              two added to reaction mixture from stage four in stage five,
              additional reactant isomer also present, alternate preparation
              also described

RX(5)    RCT  N 676130-06-6
         RGT  Y 7647-01-0 HCl
         PRO  T 151052-40-3
         SOL  7732-18-5 Water, 64-17-5 EtOH
         CON  3 hours, room temperature -> 45 deg C
         NTE  alternate preparations also described


RX(11) OF 13 COMPOSED OF RX(7), RX(8)
RX(11)   AA  +  M  ===>  AD
```





AD

RX(7)

STAGE(1)
RGT D 7439-95-4 Mg
SOL 109-99-9 THF
CON room temperature -> 14 deg C

STAGE(2)
RGT U 1191-15-7 AlH(Bu-i)2
SOL 108-88-3 PhMe
CON 20 minutes, 14 deg C

STAGE(3)
RCT AA 17100-68-4
CON SUBSTAGE(1) 14 deg C
SUBSTAGE(2) 40 minutes, 14 deg C
SUBSTAGE(3) 2.5 hours, 25 deg C

STAGE(4)
RCT M 676130-00-0
RGT E 7646-85-7 ZnCl2
CAT 15629-92-2 Ni complex
SOL 109-99-9 THF
CON room temperature -> 15 deg C

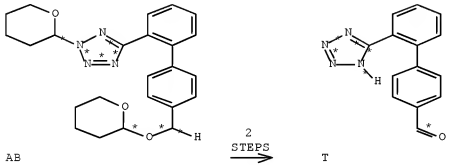
STAGE(5)
CON SUBSTAGE(1) 1 hour, <25 deg C
SUBSTAGE(2) 17.5 hours, room temperature

PRO AB 862802-05-9
NTE Grignard reaction first three stages, Grignard reagent from stage three added to reaction mixture from stage four in stage five, additional reactant isomer also present

RX(8) RCT AB 862802-05-9

STAGE(1)
RGT V 7664-93-9 H2SO4
SOL 7732-18-5 Water, 64-17-5 EtOH
CON 3.5 hours, room temperature -> 45 deg C

```
            STAGE(2)
               SOL  7732-18-5 Water
               CON  SUBSTAGE(1) 45 deg C
                    SUBSTAGE(2) 45 deg C -> room temperature

            STAGE(3)
               RGT  AE 1310-73-2 NaOH
               SOL  7732-18-5 Water
               CON  room temperature, pH 2 - 3

          PRO  AD 160514-13-6


RX(12) OF 13 COMPOSED OF RX(8), RX(9)
RX(12)    AB  ===>  T
```




```
RX(8)     RCT  AB 862802-05-9

            STAGE(1)
               RGT  V 7664-93-9 H2SO4
               SOL  7732-18-5 Water, 64-17-5 EtOH
               CON  3.5 hours, room temperature -> 45 deg C

            STAGE(2)
               SOL  7732-18-5 Water
               CON  SUBSTAGE(1) 45 deg C
                    SUBSTAGE(2) 45 deg C -> room temperature

            STAGE(3)
               RGT  AE 1310-73-2 NaOH
               SOL  7732-18-5 Water
               CON  room temperature, pH 2 - 3

          PRO  AD 160514-13-6

RX(9)     RCT  AD 160514-13-6

            STAGE(1)
               RGT  AF 67-68-5 DMSO, AG 121-44-8 Et3N
               CON  room temperature -> 12 deg C

            STAGE(2)
               RGT  AH 28322-92-1 Pyridine-SO3
               SOL  67-68-5 DMSO
```

CON 10 minutes, 12 deg C

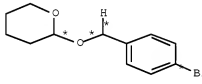
STAGE(3)
RGT AG 121-44-8 Et3N
CON <48 hours, room temperature

STAGE(4)
SOL 141-78-6 AcOEt
CON room temperature -> 5 deg C

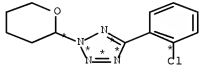
STAGE(5)
RGT Y 7647-01-0 HCl
SOL 7732-18-5 Water

PRO T 151052-40-3
NTE alternate preparations also described

RX(13) OF 13 COMPOSED OF RX(7), RX(8), RX(9)
RX(13) AA + M ===> T

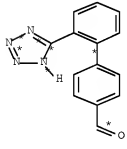


AA



M

3
STEPS



T

RX(7)

STAGE(1)
RGT D 7439-95-4 Mg
SOL 109-99-9 THF
CON room temperature -> 14 deg C

STAGE(2)
RGT U 1191-15-7 AlH(Bu-i)2
SOL 108-88-3 PhMe
CON 20 minutes, 14 deg C

```
            STAGE(3)
               RCT  AA 17100-68-4
               CON  SUBSTAGE(1) 14 deg C
                    SUBSTAGE(2) 40 minutes, 14 deg C
                    SUBSTAGE(3) 2.5 hours, 25 deg C

            STAGE(4)
               RCT  M 676130-00-0
               RGT  E 7646-85-7 ZnCl2
               CAT  15629-92-2 Ni complex
               SOL  109-99-9 THF
               CON  room temperature -> 15 deg C

            STAGE(5)
               CON  SUBSTAGE(1) 1 hour, <25 deg C
                    SUBSTAGE(2) 17.5 hours, room temperature

          PRO  AB 862802-05-9
          NTE  Grignard reaction first three stages, Grignard reagent from
               stage three added to reaction mixture from stage four in stage
               five, additional reactant isomer also present

RX(8)     RCT  AB 862802-05-9

            STAGE(1)
               RGT  V 7664-93-9 H2SO4
               SOL  7732-18-5 Water, 64-17-5 EtOH
               CON  3.5 hours, room temperature -> 45 deg C

            STAGE(2)
               SOL  7732-18-5 Water
               CON  SUBSTAGE(1) 45 deg C
                    SUBSTAGE(2) 45 deg C -> room temperature

            STAGE(3)
               RGT  AE 1310-73-2 NaOH
               SOL  7732-18-5 Water
               CON  room temperature, pH 2 - 3

          PRO  AD 160514-13-6

RX(9)     RCT  AD 160514-13-6

            STAGE(1)
               RGT  AF 67-68-5 DMSO, AG 121-44-8 Et3N
               CON  room temperature -> 12 deg C

            STAGE(2)
               RGT  AH 28322-92-1 Pyridine-SO3
               SOL  67-68-5 DMSO
               CON  10 minutes, 12 deg C

            STAGE(3)
               RGT  AG 121-44-8 Et3N
               CON  <48 hours, room temperature

            STAGE(4)
               SOL  141-78-6 AcOEt
               CON  room temperature -> 5 deg C
```

STAGE(5)
RGT Y 7647-01-0 HCl
SOL 7732-18-5 Water

PRO T 151052-40-3
NTE alternate preparations also described
IN Krell, Christoph; Hirt, Hans

L45 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:267315 CAPLUS Full-text
DOCUMENT NUMBER: 140:287711
TITLE: Process for the manufacture of valsartan
INVENTOR(S): Denni-Dischert, Donatienne; Hirt, Hans; Neville, Dan; Sedelmeier, Gottfried; Schnyder, Anita; Derrien, Nadine; Kaufmann, Daniel
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026847	A1	20040401	WO 2003-EP10543	20030922
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2502629	A1	20040401	CA 2003-2502629	20030922
AU 2003270241	A1	20040408	AU 2003-270241	20030922
AU 2003270241	B2	20070823		
BR 2003014132	A	20050628	BR 2003-14132	20030922
EP 1546122	A1	20050629	EP 2003-750599	20030922
EP 1546122	B1	20071121		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1688556	A	20051026	CN 2003-824514	20030922
CN 100357279	C	20071226		
JP 2006502178	T	20060119	JP 2004-537146	20030922
EP 1878729	A1	20080116	EP 2007-113176	20030922
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CN 101153027	A	20080402	CN 2007-10169252	20030922
ES 2295623	T3	20080416	ES 2003-750599	20030922
NZ 538927	A	20080530	NZ 2003-538927	20030922
RU 2348619	C2	20090310	RU 2005-112444	20030922
ZA 2005002159	A	20050921	ZA 2005-2159	20050315
IN 2005CN00421	A	20070427	IN 2005-CN421	20050318
MX 2005003140	A	20050622	MX 2005-3140	20050322

NO 2005001970	A	20050616	NO 2005-1970		20050422
US 20060069268	A1	20060330	US 2005-528323		20050505
HK 1079771	A1	20080627	HK 2005-111768		20051220
IN 2007CN01210	A	20070831	IN 2007-CN1210		20070322
AU 2007234598	A1	20071213	AU 2007-234598		20071122
PRIORITY APPLN. INFO.:			GB 2002-22056	A	20020923
			AU 2003-270241	A3	20030922
			CN 2003-824514	A3	20030922
			EP 2003-750599	A3	20030922
			WO 2003-EP10543	W	20030922
			IN 2005-CN421	A3	20050318

OTHER SOURCE(S): MARPAT 140:287711

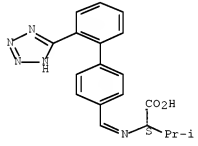
AB A process for the manufacture of valsartan is reported. Thus, L-valine was treated with 2'-(1H-tetrazol-5-yl)biphenyl-4-carboxaldehyde to give the imine which was reduced with NaBH4 and acylated with BuCOCl.

IT 676129-91-2P 676129-92-3P 676130-02-2P
676130-03-3P 676130-06-6P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for the manufacture of valsartan)

RN 676129-91-2 CAPLUS

CN L-Valine, N-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methylene]- (9CI) (CA INDEX NAME)

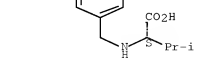
Absolute stereochemistry.
Double bond geometry unknown.



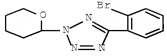
RN 676129-92-3 CAPLUS

CN L-Valine, N-[[2'-(2H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 676130-02-2 CAPLUS
CN 2H-Tetrazole, 5-(2-bromophenyl)-2-(tetrahydro-2H-pyran-2-yl)- (CA INDEX NAME)



RN 676130-03-3 CAPLUS
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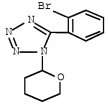
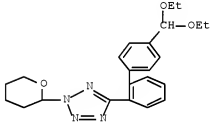
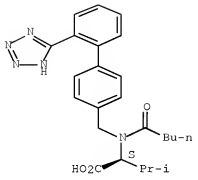


RN 676130-06-6 CAPLUS
CN 2H-Tetrazole, 5-[4'-(diethoxymethyl)[1,1'-biphenyl]-2-yl]-2-(tetrahydro-2H-pyran-2-yl)- (CA INDEX NAME)



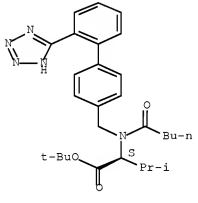
IT 137862-53-4P, Valsartan 676129-95-6P
676129-96-7P 676129-98-9P 676129-99-0P
676130-00-0P 676130-01-1P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for the manufacture of valsartan)
RN 137862-53-4 CAPLUS
CN L-Valine, N-(1-oxopentyl)-N-[[2'-(2H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



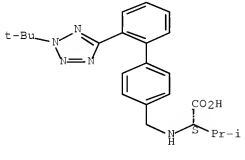
RN 676129-95-6 CAPLUS
CN L-Valine, N-(1-oxopentyl)-N-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 676129-96-7 CAPLUS
CN L-Valine, N-[[2'-[2-(1,1-dimethylethyl)-2H-tetrazol-5-yl][1,1'-biphenyl]-4-yl]methyl]- (CA INDEX NAME)

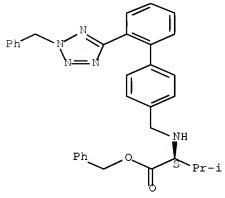
Absolute stereochemistry.



RN 676129-98-9 CAPLUS
CN L-Valine, N-[[2'-[2-(phenylmethyl)-2H-tetrazol-5-yl][1,1'-biphenyl]-4-

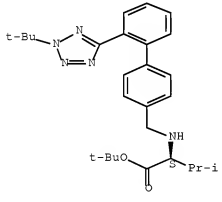
yl]methyl]-, phenylmethyl ester (CA INDEX NAME)

Absolute stereochemistry.

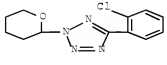


RN 676129-99-0 CAPLUS
CN L-Valine, N-[[2'-[2-(1,1-dimethylethyl)-2H-tetrazol-5-yl][1,1'-biphenyl]-4-yl]methyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

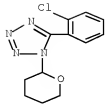
Absolute stereochemistry.



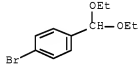
RN 676130-00-0 CAPLUS
CN 2H-Tetrazole, 5-(2-chlorophenyl)-2-(tetrahydro-2H-pyran-2-yl)- (CA INDEX NAME)



RN 676130-01-1 CAPLUS
CN 1H-Tetrazole, 5-(2-chlorophenyl)-1-(tetrahydro-2H-pyran-2-yl)- (CA INDEX NAME)



IT 34421-94-8, 4-Bromobenzaldehyde diethylacetal 50907-46-5
, 5-(2-Chlorophenyl)-1H-tetrazole 73096-42-1,
5-(2-Bromophenyl)-1H-tetrazole 151052-37-8 676129-97-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for the manufacture of valsartan)
RN 34421-94-8 CAPLUS
CN Benzene, 1-bromo-4-(diethoxymethyl)- (CA INDEX NAME)



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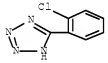

RN 73096-42-1 CAPLUS
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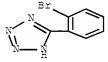

RN 151052-37-8 CAPLUS
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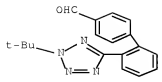

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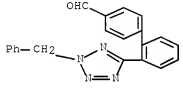
(CA INDEX NAME)



IT 137863-20-8P 151052-40-3P 676129-93-4P
676129-94-5P
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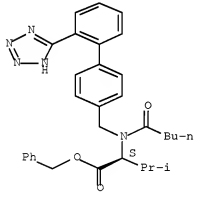
(Reactant or reagent)
(process for the manufacture of valsartan)
RN 137863-20-8 CAPLUS
CN L-Valine, N-(1-oxopentyl)-N-[[2'-(2H-tetrazol-5-yl)[1,1'-biphenyl]-4-
yl]methyl]-, phenylmethyl ester (CA INDEX NAME)

Absolute stereochemistry.



RN 151052-40-3 CAPLUS
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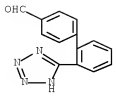

RN 676129-93-4 CAPLUS
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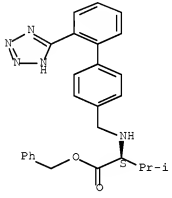
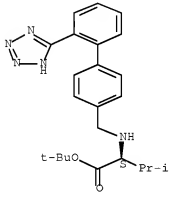
Absolute stereochemistry.



RN 676129-94-5 CAPLUS
CN L-Valine, N-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

REACTION SEARCH

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=> fil casrea; d stat que 143
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FILE CONTENT:1840 - 8 Mar 2009 VOL 150 ISS 11

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************************************************************
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*                                                          *
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L6                STR
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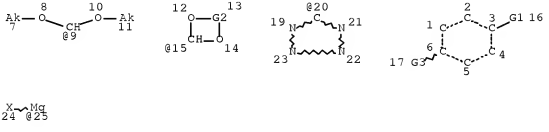


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REP G2=(2-10) CH2
VAR G3=H/X/25
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CONNECT IS E1  RC AT  11
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  24
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STEREO ATTRIBUTES: NONE
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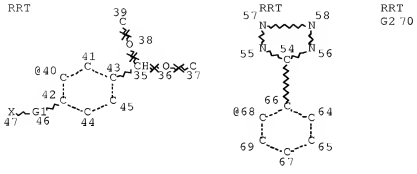
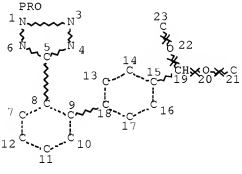
L33 STR



Page 1-A



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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 47

STEREO ATTRIBUTES: NONE
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L43 1 SEA FILE=CASREACT SUB=L40 SSS FUL L33 (4 REACTIONS)

100.0% DONE 4628 VERIFIED 4 HIT RXNS 1 DOCS
SEARCH TIME: 00.00.02

=> s l43 not l41
L46 0 L43 NOT L41 L41=INVENTOR SEARCH ANSWER SET, PREVIOUSLY PRINTED

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=> fil reg; d stat que l11; d stat que l17; d que nos l19; fil capl; d que nos l25;
s l25 not l30
FILE 'REGISTRY' ENTERED AT 10:50:31 ON 12 MAR 2009
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STRUCTURE FILE UPDATES:   11 MAR 2009  HIGHEST RN 1119363-64-2
DICTIONARY FILE UPDATES:  11 MAR 2009  HIGHEST RN 1119363-64-2

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L6                STR
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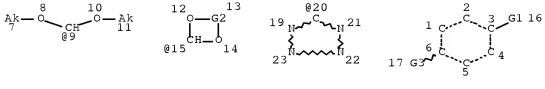


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REP G2=(2-10) CH2
VAR G3=H/X/25
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CONNECT IS E1  RC AT  11
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  24

STEREO ATTRIBUTES: NONE
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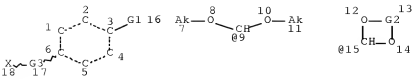

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REP G2=(2-10) CH2
REP G3=(0-1) MG
NODE ATTRIBUTES:
CONNECT IS E1  RC AT   7
CONNECT IS E1  RC AT  11
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
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STEREO ATTRIBUTES: NONE
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100.0% PROCESSED    1263 ITERATIONS                          300 ANSWERS
SEARCH TIME: 00.00.01
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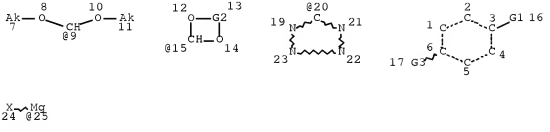
L6 STR



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REP G2=(2-10) CH2
VAR G3=H/X/25
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CONNECT IS E1  RC AT  11
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
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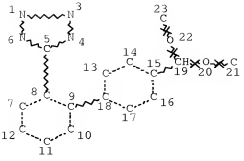

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GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
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100.0% PROCESSED 15974 ITERATIONS 10 ANSWERS
SEARCH TIME: 00.00.01

L6 STR
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L12 STR
L17 10 SEA FILE=REGISTRY SUB=L8 SSS FUL L12
L18 300689 SEA FILE=REGISTRY SPE=ON ABB=ON 16.525/RID AND 46.150.18/RID

L19 56716 SEA FILE=REGISTRY SPE=ON ABB=ON L8 AND L18 NOT L17

FILE 'CAPLUS' ENTERED AT 10:50:31 ON 12 MAR 2009
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FILE COVERS 1907 - 12 Mar 2009 VOL 150 ISS 11
FILE LAST UPDATED: 11 Mar 2009 (20090311/ED)

Caplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.

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substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

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L12             STR
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L18      300689 SEA FILE=REGISTRY SPE=ON  ABB=ON  16.525/RID AND 46.150.18/RID

L19       56716 SEA FILE=REGISTRY SPE=ON  ABB=ON  L8 AND L18 NOT L17
L21           7 SEA FILE=CAPLUS SPE=ON  ABB=ON  L17/P  /P=PREPARATION
L22         902 SEA FILE=CAPLUS SPE=ON  ABB=ON  L11
L23       15869 SEA FILE=CAPLUS SPE=ON  ABB=ON  L19
L25           7 SEA FILE=CAPLUS SPE=ON  ABB=ON  L21 AND (L22 OR L23)



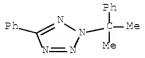
L47           5 L25 NOT L30

=> d ibib abs hitstr 147 1-5; fil hom

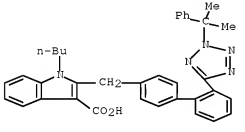
L47  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         1999:712676  CAPLUS  Full-text
DOCUMENT NUMBER:          132:107519
TITLE:                    Nucleophilic Aromatic Substitution Reactions of Novel
                          5-(2-Methoxyphenyl)tetrazole Derivatives with
                          Organolithium Reagents
AUTHOR(S):                Norman, Derek P. G.; Bunnell, Aaron E.; Stabler, S.
                          Russell; Flippin, Lee A.
CORPORATE SOURCE:         Neurobiology Unit Department of Medicinal Chemistry,
                          Roche Bioscience, Palo Alto, CA, 94304-1397, USA
SOURCE:                   Journal of Organic Chemistry (1999), 64(25), 9301-9306
                          CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER:                American Chemical Society
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
```

AB It was demonstrated that 5-aryltetrazoles protected by an N-cumyl group react with a variety of common organolithium reagents to give a facile nucleophilic aromatic substitution of either one or two nucleofugic methoxy groups situated ortho to the tetrazole ring. The employment of tetrazole protection during these reactions provides for milder and more versatile reaction conditions, as well as a generally more economical use of the organometallic reagent than was previously described for the substitution of 5-(2-fluorophenyl)-1H-tetrazole. It was also shown that the cumyl-protected tetrazole ring is generally stable under strongly basic reaction conditions, although it can be removed efficiently by hydrogenolysis or by treatment with boron trifluoride etherate in the presence of a carbocation scavenger. Thus, N-cumylation/decumylation may offer a potentially versatile new protection strategy for the tetrazole moiety.

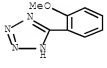
IT 165670-57-5, N(2)-Cumyl-5-phenyltetrazole 165670-66-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(nucleophilic aromatic substitution of (methoxyphenyl)tetrazole derivs. with organolithium reagents)
RN 165670-57-5 CAPLUS
CN 2H-Tetrazole, 2-(1-methyl-1-phenylethyl)-5-phenyl- (CA INDEX NAME)



RN 165670-66-6 CAPLUS
CN 1H-Indole-3-carboxylic acid, 1-butyl-2-[[2'-[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl][1,1'-biphenyl]-4-yl]methyl]- (CA INDEX NAME)



IT 51449-81-1P, 5-(2-Methoxyphenyl)-1H-tetrazole 165670-61-1P
188890-66-6P, 5-(2,6-Dimethoxyphenyl)-1H-tetrazole
255727-87-8P, 5-(2,3-Dimethoxyphenyl)-1H-tetrazole
255727-88-9P 255727-89-0P 255727-94-7P
255728-01-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(nucleophilic aromatic substitution of (methoxyphenyl)tetrazole derivs. with organolithium reagents)
RN 51449-81-1 CAPLUS
CN 2H-Tetrazole, 5-(2-methoxyphenyl)- (CA INDEX NAME)



RN 165670-61-1 CAPLUS
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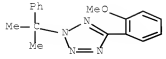
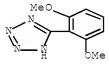


RN 188890-66-6 CAPLUS
CN 2H-Tetrazole, 5-(2,6-dimethoxyphenyl)- (CA INDEX NAME)



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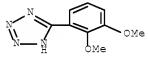

RN 255727-88-9 CAPLUS
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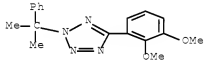

RN 255727-89-0 CAPLUS
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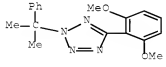

RN 255727-94-7 CAPLUS
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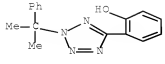

RN 255728-01-9 CAPLUS
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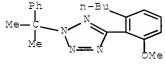
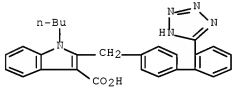
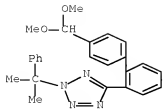


IT 149652-34-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(nucleophilic aromatic substitution of (methoxyphenyl)tetrazole derivs. with organolithium reagents)
RN 149652-34-6 CAPLUS
CN 1H-Indole-3-carboxylic acid, 1-butyl-2-[[2'-(2H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (CA INDEX NAME)

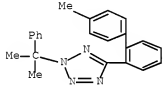


IT 18039-42-4P, 5-Phenyl-1H-tetrazole 174001-65-1P
179089-07-7P 255727-90-3P 255727-91-4P
255727-92-5P 255727-95-8P 255727-97-0P
255727-99-2P 255728-03-1P 255728-04-2P
255728-06-4P 255728-07-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 18039-42-4 CAPLUS
CN 2H-Tetrazole, 5-phenyl- (CA INDEX NAME)

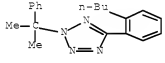
RN 174001-65-1 CAPLUS
CN 2H-Tetrazole, 5-[4'-(dimethoxymethyl)[1,1'-biphenyl]-2-yl]-2-(1-methyl-1-phenylethyl)- (CA INDEX NAME)



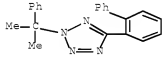
RN 179089-07-7 CAPLUS
CN 2H-Tetrazole, 5-(4'-methyl[1,1'-biphenyl]-2-yl)-2-(1-methyl-1-phenylethyl)-
(CA INDEX NAME)



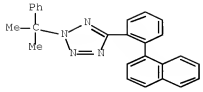
RN 255727-90-3 CAPLUS
CN 2H-Tetrazole, 5-(2-butylphenyl)-2-(1-methyl-1-phenylethyl)- (CA INDEX
NAME)



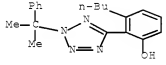
RN 255727-91-4 CAPLUS
CN 2H-Tetrazole, 5-[1,1'-biphenyl]-2-yl-2-(1-methyl-1-phenylethyl)- (CA
INDEX NAME)



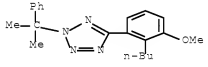
RN 255727-92-5 CAPLUS
CN 2H-Tetrazole, 2-(1-methyl-1-phenylethyl)-5-[2-(1-naphthalenyl)phenyl]-
(CA INDEX NAME)



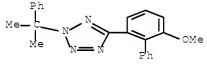
RN 255727-95-8 CAPLUS
CN Phenol, 3-butyl-2-[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



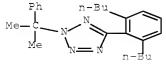
RN 255727-97-0 CAPLUS
CN 2H-Tetrazole, 5-(2-butyl-3-methoxyphenyl)-2-(1-methyl-1-phenylethyl)- (CA INDEX NAME)



RN 255727-99-2 CAPLUS
CN 2H-Tetrazole, 5-(6-methoxy[1,1'-biphenyl]-2-yl)-2-(1-methyl-1-phenylethyl)- (CA INDEX NAME)

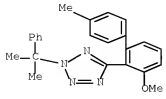


RN 255728-03-1 CAPLUS
CN 2H-Tetrazole, 5-(2,6-dibutylphenyl)-2-(1-methyl-1-phenylethyl)- (CA INDEX NAME)

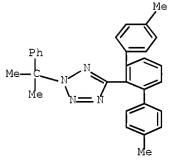


RN 255728-04-2 CAPLUS

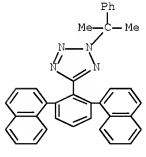
CN 2H-Tetrazole, 5-(3-methoxy-4'-methyl[1,1'-biphenyl]-2-yl)-2-(1-methyl-1-phenylethyl)- (CA INDEX NAME)



RN 255728-06-4 CAPLUS
CN 2H-Tetrazole, 2-(1-methyl-1-phenylethyl)-5-(4,4''-dimethyl[1,1':3',1''-terphenyl]-2'-yl)- (9CI) (CA INDEX NAME)



RN 255728-07-5 CAPLUS
CN 2H-Tetrazole, 5-(2,6-di-1-naphthalenylphenyl)-2-(1-methyl-1-phenylethyl)- (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:1006744 CAPLUS Full-text
DOCUMENT NUMBER: 124:176118
ORIGINAL REFERENCE NO.: 124:32663a,32666a
TITLE: Process for preparing 1-butyl-2-[2'-(2H-tetrazol-5-yl)biphenyl-4-ylmethyl]-

1H-indole-3-carboxylic acid via coupling of metalated 1-butyl-1H-indole-3-carboxylic acid with protected 2'-(2H-tetrazol-5-yl)biphenyl-4-carbaldehyde

INVENTOR(S): Fisher, Lawrence E.; Flippin, Lee A.; Martin, Michael G.

PATENT ASSIGNEE(S): Syntex (U.S.A.) Inc., USA

SOURCE: U.S., 9 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

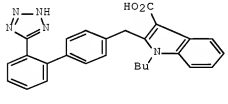
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5468867	A	19951121	US 1994-250129	19940527
CA 2191575	A1	19951207	CA 1995-2191575	19950526
WO 9532961	A1	19951207	WO 1995-US6431	19950526
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UG				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9526071	A	19951221	AU 1995-26071	19950526
ZA 9504305	A	19961126	ZA 1995-4305	19950526
EP 760814	A1	19970312	EP 1995-920592	19950526
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1149294	A	19970507	CN 1995-193256	19950526
CN 1070491	C	20010905		
BR 9507900	A	19970916	BR 1995-7900	19950526
JP 10501229	T	19980203	JP 1995-500981	19950526
IL 113877	A	19981227	IL 1995-113877	19950526

PRIORITY APPLN. INFO.: US 1994-250129 A 19940527
WO 1995-US6431 W 19950526

OTHER SOURCE(S): CASREACT 124:176118; MARPAT 124:176118

GI



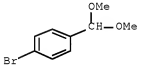
I

AB A process is claimed for the preparation of 1-butyl-2-[2'-(2H-tetrazol-5-yl)biphenyl-4-ylmethyl]-1H-indole-3- carboxylic acid (I) which process comprises: (A) (i) treating 1-butyl-1H-indole-3-carboxylic acid with an organometallic base to give 2-metalated 1-butyl-1H-indole-3-carboxylic acid, (ii) optionally treating the 2-metalated 1-butyl-1H-indole-3-carboxylic acid with a metal halide to give 2-transmetalated 1-butyl-1H-indole-3-carboxylic acid and (iii) reacting the 2-metalated or 2-transmetalated 1-butyl-1H-indole-3-carboxylic acid with protected 2'-(2H-tetrazol-5-yl)biphenyl-4-carbaldehyde to give protected 1-butyl-2-[2'-(2H-tetrazol-5-yl)biphenyl-4-

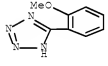
yl(hydroxy)methyl]-1H-indole-3- carboxylic acid; (B) dehydroxylating to give protected 1-butyl-2-[2'-(2H-tetrazol-5-yl)-biphenyl-4-ylmethyl]-1H-indole-3-carboxylic acid and (C) deprotecting. Thus, e.g., treatment of 1-butyl-3-indolecarboxylic acid (217 g, 1.56 mol, preparation given) with BuLi followed by 2'-[2-(triphenylmethyl)-2H-tetrazol-5-yl]biphenyl-4- carbaldehyde (292 g, 0.956 mol, preparation given) afforded 1-butyl-2-{2'-[2-(triphenylmethyl)-2H-tetrazol-5-yl]biphenyl-4- yl(hydroxy)methyl}-1H-indole-3-carboxylic acid (395.2 g, 0.56 mol); hydrogenation of the latter over 10% Pd/C afforded I (1.2 g, 2.66 mmol).

IT 24856-58-4P, 1-Bromo-4-(dimethoxymethyl)benzene
51449-81-1P, 5-(2-Methoxyphenyl)-2H-tetrazole 138804-35-0P
151052-37-8P 155982-56-5P 165670-60-0P
165670-61-1P 165670-62-2P 165670-65-6P
174001-58-2P 174001-59-3P 174001-60-6P
174001-61-7P 174001-62-8P 174001-63-9P
174001-64-0P 174001-65-1P 174001-66-2P
174001-67-3P 174001-68-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1-butyl-2-[2'-(2H-tetrazol-5-yl)biphenyl-4-ylmethyl1-1H-indole-3-carboxylic acid via coupling of metalated 1-butyl-1H-indole-3-carboxylic acid with protected 2'-(2H-tetrazol-5-yl)biphenyl-4-carbaldehyde)

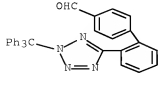
RN 24856-58-4 CAPLUS
CN Benzene, 1-bromo-4-(dimethoxymethyl)- (CA INDEX NAME)



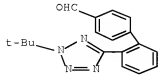
RN 51449-81-1 CAPLUS
CN 2H-Tetrazole, 5-(2-methoxyphenyl)- (CA INDEX NAME)



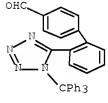
RN 138804-35-0 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(triphenylmethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



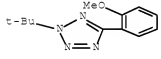
RN 151052-37-8 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(1,1-dimethylethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



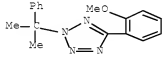
RN 155983-56-5 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[1-(triphenylmethyl)-1H-tetrazol-5-yl]- (CA INDEX NAME)



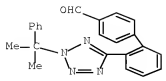
RN 165670-60-0 CAPLUS
CN 2H-Tetrazole, 2-(1,1-dimethylethyl)-5-(2-methoxyphenyl)- (CA INDEX NAME)



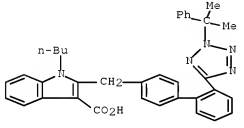
RN 165670-61-1 CAPLUS
CN 2H-Tetrazole, 5-(2-methoxyphenyl)-2-(1-methyl-1-phenylethyl)- (CA INDEX NAME)



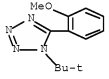
RN 165670-62-2 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



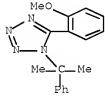
RN 165670-66-6 CAPLUS
CN 1H-Indole-3-carboxylic acid, 1-butyl-2-[[2'-[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl][1,1'-biphenyl]-4-yl]methyl]- (CA INDEX NAME)



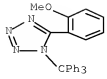
RN 174001-58-2 CAPLUS
CN 1H-Tetrazole, 1-(1,1-dimethylethyl)-5-(2-methoxyphenyl)- (CA INDEX NAME)



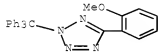
RN 174001-59-3 CAPLUS
CN 1H-Tetrazole, 5-(2-methoxyphenyl)-1-(1-methyl-1-phenylethyl)- (CA INDEX NAME)



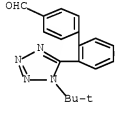
RN 174001-60-6 CAPLUS
CN 1H-Tetrazole, 5-(2-methoxyphenyl)-1-(triphenylmethyl)- (CA INDEX NAME)



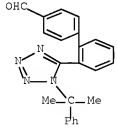
RN 174001-61-7 CAPLUS
CN 2H-Tetrazole, 5-(2-methoxyphenyl)-2-(triphenylmethyl)- (CA INDEX NAME)



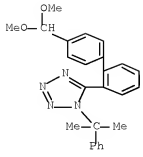
RN 174001-62-8 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[1-(1,1-dimethylethyl)-1H-tetrazol-5-yl]- (CA INDEX NAME)



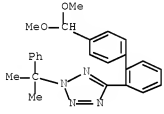
RN 174001-63-9 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[1-(1-methyl-1-phenylethyl)-1H-tetrazol-5-yl]- (CA INDEX NAME)



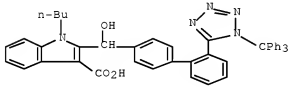
RN 174001-64-0 CAPLUS
CN 1H-Tetrazole, 5-[4'-(dimethoxymethyl)[1,1'-biphenyl]-2-yl]-1-(1-methyl-1-phenylethyl)- (CA INDEX NAME)



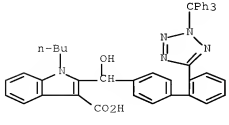
RN 174001-65-1 CAPLUS
CN 2H-Tetrazole, 5-[4'-(dimethoxymethyl)[1,1'-biphenyl]-2-yl]-2-(1-methyl-1-phenylethyl)- (CA INDEX NAME)



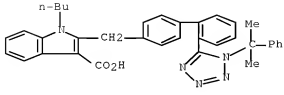
RN 174001-66-2 CAPLUS
CN 1H-Indole-3-carboxylic acid, 1-butyl-2-[hydroxy[2'-[1-(triphenylmethyl)-1H-tetrazol-5-yl][1,1'-biphenyl]-4-yl]methyl]- (CA INDEX NAME)



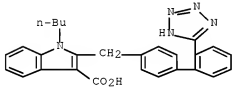
RN 174001-67-3 CAPLUS
CN 1H-Indole-3-carboxylic acid, 1-butyl-2-[hydroxy[2'-[2-(triphenylmethyl)-2H-tetrazol-5-yl][1,1'-biphenyl]-4-yl]methyl]- (CA INDEX NAME)



RN 174001-68-4 CAPLUS
CN 1H-Indole-3-carboxylic acid, 1-butyl-2-[[2'-[1-(1-methyl-1-phenylethyl)-1H-tetrazol-5-yl][1,1'-biphenyl]-4-yl]methyl]- (CA INDEX NAME)



IT 149652-34-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of 1-butyl-2-[2'-(2H-tetrazol-5-yl)biphenyl-4-ylmethyl]-1H-indole-3-carboxylic acid via coupling of metalated 1-butyl-1H-indole-3-carboxylic acid with protected 2'-(2H-tetrazol-5-yl)biphenyl-4-carbaldehyde)
RN 149652-34-6 CAPLUS
CN 1H-Indole-3-carboxylic acid, 1-butyl-2-[[2'-(2H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

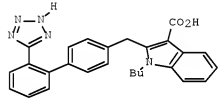
L47 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:608022 CAPLUS Full-text
DOCUMENT NUMBER: 123:112067
ORIGINAL REFERENCE NO.: 123:20024h,20025a
TITLE: Processes for preparing 1-butyl-2-[2'-(2H-tetrazol-5-yl)biphenyl-4-ylmethyl]-1H-indole-3-carboxylic acid involving deprotection of protected tetrazole with a Lewis acid in presence of a thiol
INVENTOR(S): Clark, Robin D.; Fisher, Lawrence E.; Flippin, Lee A.; Martin, Michael G.; Stabler, Stephen R.
PATENT ASSIGNEE(S): Syntex (U.S.A.) Inc., USA
SOURCE: U.S., 12 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5412102	A	19950502	US 1994-250397	19940527

US 5446121	A	19950829	US 1995-373677	19950117	
US 5527918	A	19960618	US 1995-440040	19950512	
CA 2191576	A1	19951207	CA 1995-2191576	19950526	
WO 9532962	A1	19951207	WO 1995-US6432	19950526	
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UG					
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9526439	A	19951221	AU 1995-26439	19950526	
ZA 9504306	A	19961126	ZA 1995-4306	19950526	
EP 760815	A1	19970312	EP 1995-921335	19950526	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
CN 1149293	A	19970507	CN 1995-193255	19950526	
CN 1070193	C	20010829			
BR 9507771	A	19970819	BR 1995-7771	19950526	
JP 10501230	T	19980203	JP 1996-500982	19950526	
IL 131709	A	20010430	IL 1995-131709	19950526	
IL 113876	A	20010826	IL 1995-113876	19950526	
PRIORITY APPLN. INFO.:			US 1994-250397	A3 19940527	
			US 1995-373677	A3 19950117	
			IL 1995-113876	A3 19950526	
			WO 1995-US6432	W 19950526	

OTHER SOURCE(S): CASREACT 123:112067; MARPAT 123:112067

GI



I

AB The preparation of 1-butyl-2-[2'-(2H-tetrazol-5-yl)biphenyl-4-ylmethyl]-1H-indole-3-carboxylic acid (I) comprises: (A) (i) treating protected 5-phenyl-2H-tetrazole with an organometallic base to give ortho-metalated protected 5-phenyl-2H-tetrazole, (ii) optionally treating the ortho-metalated protected 5-phenyl-2H-tetrazole with a metal halide to give ortho-transmetalated protected 5-phenyl-2H-tetrazole, (iii) reacting the ortho-metalated or ortho-transmetalated protected 5-phenyl-2H-tetrazole, optionally in the presence of phosphinated nickel or palladium catalyst, with 4-XC6H4CO2R1 in which X is halo and R1 is (C1-4)alkyl, to give protected 2'- (2H-tetrazol-5-yl) biphenyl-4-carboxylic acid (C1-4) alkyl ester, (iv) reducing the protected 2'-(2H-tetrazol-5-yl)biphenyl-4-carboxylic acid (C1-4)alkyl ester to give protected 2'-(2H-tetrazol-5-yl)biphenyl-4-methanol, and (v) halogenating the protected 2'-(2H-tetrazol-5-yl)biphenyl-4-methanol to give protected 4-halomethyl-2'-(2H-tetrazol-5-yl) biphenyl; (B) reacting the protected 4-halomethyl-2'-(2H-tetrazol-5-yl)biphenyl, optionally in the presence of phosphinated nickel or palladium catalyst, with 2-metalated or 2-transmetalated 1-but-1-yl-1H-indole-3-carboxylic acid to give protected 1-butyl-2-[2'-(2H-tetrazol-5-yl)biphenyl-4-ylmethyl]-1H-indole-3- carboxylic acid; and (C) deprotecting. Thus, e.g., treatment of protected I [1-butyl-2-{2'-[2-(1-methyl-1-phenylethyl)-2H-

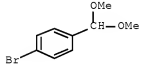
tetrazol-5-yl]-biphenyl-4- ylmethyl}-1H-indole-3-carboxylic acid, 8.0 g, 0.0141 mol, preparation given] with pentaerythritol tetrakis(2-mercaptoacetate) (4.84 mL, 0.0155 mol) and boron trifluoride etherate (6.92 mL, 0.056 mol) in 120 mL MeCN at room temperature for 1.5 h afforded I (5.9 g, 0.0131 mol).

IT 18039-42-4, 5-Phenyl-2H-tetrazole
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 1-butyl-2-[2'-(2H-tetrazol-5-yl)biphenyl-4-ylmethyl]-1H-indole-3-carboxylic acid involving deprotection of protected tetrazole with a Lewis acid in presence of a thiol)

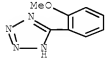
RN 18039-42-4 CAPLUS
CN 2H-Tetrazole, 5-phenyl- (CA INDEX NAME)

IT 24856-58-4P, 1-Bromo-4-(dimethoxymethyl)benzene
51449-81-1P, 5-(2-Methoxyphenyl)-2H-tetrazole 138804-35-0P
151052-37-8P 151052-38-9P 165670-57-5P
165670-58-6P 165670-60-0P 165670-61-1P
165670-62-2P 165670-63-3P 165670-64-4P
165670-66-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1-butyl-2-[2'-(2H-tetrazol-5-yl)biphenyl-4-ylmethyl]-1H-indole-3-carboxylic acid involving deprotection of protected tetrazole with a Lewis acid in presence of a thiol)

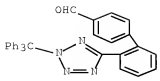
RN 24856-58-4 CAPLUS
CN Benzene, 1-bromo-4-(dimethoxymethyl)- (CA INDEX NAME)



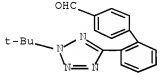
RN 51449-81-1 CAPLUS
CN 2H-Tetrazole, 5-(2-methoxyphenyl)- (CA INDEX NAME)



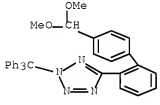
RN 138804-35-0 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(triphenylmethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



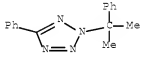
RN 151052-37-8 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(1,1-dimethylethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



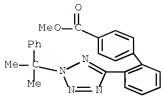
RN 151052-38-9 CAPLUS
CN 2H-Tetrazole, 5-[4'-(dimethoxymethyl)[1,1'-biphenyl]-2-yl]-2-(triphenylmethyl)- (CA INDEX NAME)



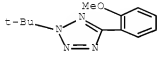
RN 165670-57-5 CAPLUS
CN 2H-Tetrazole, 2-(1-methyl-1-phenylethyl)-5-phenyl- (CA INDEX NAME)



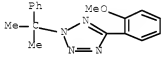
RN 165670-58-6 CAPLUS
CN [1,1'-Biphenyl]-4-carboxylic acid, 2'-[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]-, methyl ester (CA INDEX NAME)



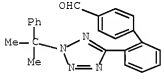
RN 165670-60-0 CAPLUS
CN 2H-Tetrazole, 2-(1,1-dimethylethyl)-5-(2-methoxyphenyl)- (CA INDEX NAME)



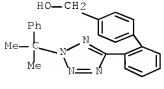
RN 165670-61-1 CAPLUS
CN 2H-Tetrazole, 5-(2-methoxyphenyl)-2-(1-methyl-1-phenylethyl)- (CA INDEX NAME)



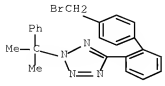
RN 165670-62-2 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



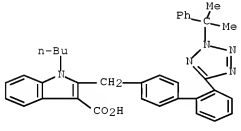
RN 165670-63-3 CAPLUS
CN [1,1'-Biphenyl]-4-methanol, 2'-[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



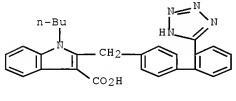
RN 165670-64-4 CAPLUS
CN 2H-Tetrazole, 5-[4'-(bromomethyl)[1,1'-biphenyl]-2-yl]-2-(1-methyl-1-phenylethyl)- (CA INDEX NAME)



RN 165670-66-6 CAPLUS
CN 1H-Indole-3-carboxylic acid, 1-butyl-2-[[2'-[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl][1,1'-biphenyl]-4-yl]methyl]- (CA INDEX NAME)



IT 149652-34-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of 1-butyl-2-[2'-(2H-tetrazol-5-yl)biphenyl-4-ylmethyl]-1H-indole-3-carboxylic acid involving deprotection of protected tetrazole with a Lewis acid in presence of a thiol)
RN 149652-34-6 CAPLUS
CN 1H-Indole-3-carboxylic acid, 1-butyl-2-[[2'-(2H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (CA INDEX NAME)



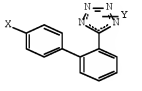
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1993:671171 CAPLUS Full-text
DOCUMENT NUMBER: 119:271171
ORIGINAL REFERENCE NO.: 119:48533a,48536a
TITLE: Preparation of 2-(5-tetrazolyl)biphenyls
INVENTOR(S): Daumas, Marc; Hoornaert, Christian; Chekroun, Isaac; Bedoya-Zurita, Manuel; Ruiz-Montes, Jose; Greciet, Helene; Rossey, Guy

PATENT ASSIGNEE(S): Synthelabo S. A., Fr.
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 550313	A1	19930707	EP 1992-403477	19921218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
FR 2685697	A1	19930702	FR 1991-16290	19911230
FR 2685697	B1	19940204		
FR 2688503	A1	19930917	FR 1992-3113	19920316
JP 05271205	A	19931019	JP 1992-348558	19921228
CA 2086364	A1	19930701	CA 1992-2086364	19921229
US 5371233	A	19941206	US 1992-998055	19921229
PRIORITY APPLN. INFO.:			FR 1991-16290 A	19911230
			FR 1992-3113 A	19920316

OTHER SOURCE(S): MARPAT 119:271171
GI

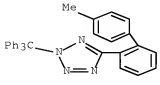


I

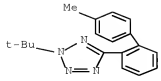
AB Title compds. {I; X = CHBr2, CHO, alkyl, CH(OR5)2, CH(OH)BR5; R5 = H, alkyl, etc.; Y = H, CMe3, CPh3, SnMe3, etc.; dashed line indicates optional position of double bonds] were prepared Thus, 4-BrC6H4Me was condensed with 5-(2-iodophenyl)-2-triphenylmethyl-2H-tetrazole and the product brominated to give I (X = CHBr2, Y = 2-CPh3).

IT 133909-97-4P 151052-35-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of tetrazolylbiphenyl)

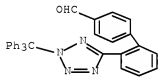
RN 133909-97-4 CAPLUS
CN 2H-Tetrazole, 5-(4'-methyl[1,1'-biphenyl]-2-yl)-2-(triphenylmethyl)- (CA INDEX NAME)



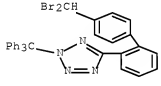
RN 151052-35-6 CAPLUS
CN 2H-Tetrazole, 2-(1,1-dimethylethyl)-5-(4'-methyl[1,1'-biphenyl]-2-yl)- (CA INDEX NAME)



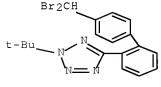
IT 138804-35-0P 151052-34-5P 151052-36-7P
151052-37-8P 151052-38-9P 151052-39-0P
151052-40-3P 151052-41-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 138804-35-0 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(triphenylmethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



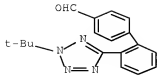
RN 151052-34-5 CAPLUS
CN 2H-Tetrazole, 5-[4'-(dibromomethyl)[1,1'-biphenyl]-2-yl]-2-(triphenylmethyl)- (CA INDEX NAME)



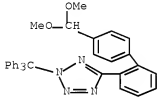
RN 151052-36-7 CAPLUS
CN 2H-Tetrazole, 5-[4'-(dibromomethyl)[1,1'-biphenyl]-2-yl]-2-(1,1-dimethylethyl)- (CA INDEX NAME)



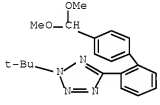
RN 151052-37-8 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(1,1-dimethylethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



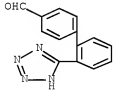
RN 151052-38-9 CAPLUS
CN 2H-Tetrazole, 5-[4'-(dimethoxymethyl)[1,1'-biphenyl]-2-yl]-2-(triphenylmethyl)- (CA INDEX NAME)



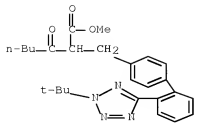
RN 151052-39-0 CAPLUS
CN 2H-Tetrazole, 5-[4'-(dimethoxymethyl)[1,1'-biphenyl]-2-yl]-2-(1,1-dimethylethyl)- (CA INDEX NAME)



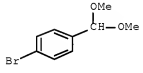
RN 151052-40-3 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-(2H-tetrazol-5-yl)- (CA INDEX NAME)



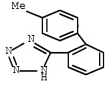
RN 151052-41-4 CAPLUS
CN [1,1'-Biphenyl]-4-propanoic acid, 2'-[2-(1,1-dimethylethyl)-2H-tetrazol-5-yl]-α-(1-oxopentyl)-, methyl ester (CA INDEX NAME)



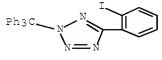
IT 24856-58-4, 1-Bromo-4-dimethoxymethylbenzene 120568-11-8
145337-52-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of tetrazolylbiphenyl)
RN 24856-58-4 CAPLUS
CN Benzene, 1-bromo-4-(dimethoxymethyl)- (CA INDEX NAME)



RN 120568-11-8 CAPLUS
CN 2H-Tetrazole, 5-(4'-methyl[1,1'-biphenyl]-2-yl)- (CA INDEX NAME)



RN 145337-52-6 CAPLUS
CN 2H-Tetrazole, 5-(2-iodophenyl)-2-(triphenylmethyl)- (CA INDEX NAME)

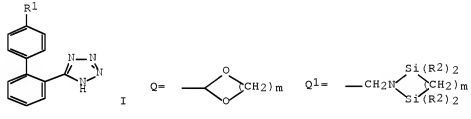


L47 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1993:560296 CAPLUS Full-text
DOCUMENT NUMBER: 119:160296
ORIGINAL REFERENCE NO.: 119:28733a,28736a
TITLE: Process for the preparation of substituted biphenyltetrazoles

INVENTOR(S): Murray, William V.; Russell, Ronald
PATENT ASSIGNEE(S): Ortho Pharmaceutical Corp., USA
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 540356	A2	19930505	EP 1992-309968	19921030
EP 540356	A3	19930825		
EP 540356	B1	19990324		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5252753	A	19931012	US 1991-786666	19911101
AU 9227404	A	19930506	AU 1992-27404	19921028
AU 651014	B2	19940707		
CA 2081847	A1	19930502	CA 1992-2081847	19921030
JP 05279350	A	19931026	JP 1992-315657	19921030
JP 3145813	B2	20010312		
AT 178058	T	19990415	AT 1992-309968	19921030
ES 2130161	T3	19990701	ES 1992-309968	19921030

PRIORITY APPLN. INFO.: US 1991-786666 A 19911101
OTHER SOURCE(S): MARPAT 119:160296
GI



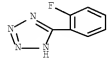
I

AB Title compds. I (R1 = (R2O)2CH, R2OCH2, [(R2)3Si]2NCH2, (R2)2C:CH, R2C.tplbond.C, C1-4 alkyl wherein R2 = C1-3 alkyl, Q, Q1, m = 2-4; n = 1-3] useful as angiotensin II antagonists (no data) are preparation by reaction of 2-fluorophenyl-1H-tetrazole (II) with a Grignard reagent R1C6H4MgX wherein X = Cl, Br, iodine. II (preparation given) was treated with p-MeO6H4MgBr to give after workup I (R1 = Me).

IT 50907-19-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and Grignard alkylation of, with tolylmagnesium bromide)

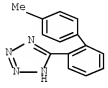
RN 50907-19-2 CAPLUS

CN 2H-Tetrazole, 5-(2-fluorophenyl)- (CA INDEX NAME)

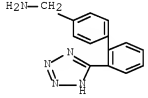


IT 120568-11-8P 147225-68-1P 150045-49-1P
150045-50-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as angiotensin II antagonist)

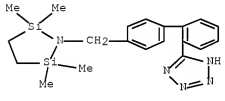
RN 120568-11-8 CAPLUS
CN 2H-Tetrazole, 5-(4'-methyl[1,1'-biphenyl]-2-yl)- (CA INDEX NAME)



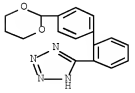
RN 147225-68-1 CAPLUS
CN [1,1'-Biphenyl]-4-methanamine, 2'-(2H-tetrazol-5-yl)- (CA INDEX NAME)



RN 150045-49-1 CAPLUS
CN 2H-Tetrazole, 5-[4'-[(2,2,5,5-tetramethyl-1-aza-2,5-disilacyclopent-1-yl)methyl][1,1'-biphenyl]-2-yl]- (CA INDEX NAME)



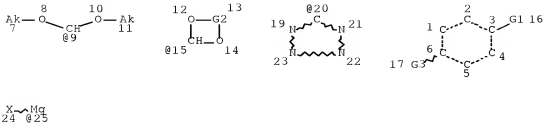
RN 150045-50-4 CAPLUS
CN 2H-Tetrazole, 5-[4'-(1,3-dioxan-2-yl)[1,1'-biphenyl]-2-yl]- (CA INDEX NAME)



FILE 'HOME' ENTERED AT 10:50:48 ON 12 MAR 2009

SEARCH HISTORY

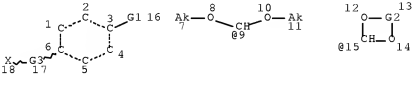
=> d stat que l11; d stat que l17;d stat que l43;d his nofile
L6 STR



VAR G1=9/15/20
REP G2=(2-10) CH2
VAR G3=H/X/25
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 7
CONNECT IS E1 RC AT 11
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE
L8 61787 SEA FILE=REGISTRY SSS FUL L6
L9 STR



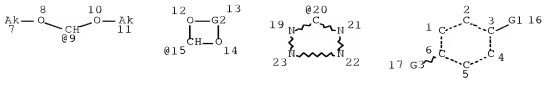
VAR G1=9/15
REP G2=(2-10) CH2
REP G3=(0-1) MG
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 7
CONNECT IS E1 RC AT 11
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE
L11 300 SEA FILE=REGISTRY SUB=L8 SSS FUL L9

100.0% PROCESSED 1263 ITERATIONS 300 ANSWERS
SEARCH TIME: 00.00.01

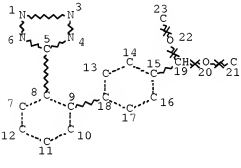
L6 STR



VAR G1=9/15/20
REP G2=(2-10) CH2
VAR G3=H/X/25
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 7
CONNECT IS E1 RC AT 11
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE
L8 61787 SEA FILE=REGISTRY SSS FUL L6
L12 STR



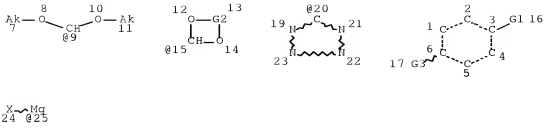
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
L17 10 SEA FILE=REGISTRY SUB=L8 SSS FUL L12

100.0% PROCESSED 15974 ITERATIONS 10 ANSWERS
SEARCH TIME: 00.00.01

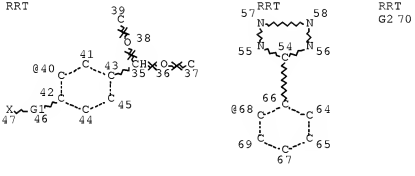
L6 STR



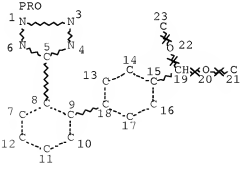
VAR G1=9/15/20
REP G2=(2-10) CH2
VAR G3=H/X/25
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 7
CONNECT IS E1 RC AT 11
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE
L8 61787 SEA FILE=REGISTRY SSS FUL L6
L33 STR



Page 1-A



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Page 2-A
REP G1=(0-1) MG
VAR G2=40/68
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  47

STEREO ATTRIBUTES: NONE
L40         3772 SEA FILE=CASREACT SPE=ON  ABB=ON  L8
L43            1 SEA FILE=CASREACT SUB=L40 SSS FUL L33 (     4 REACTIONS)

100.0% DONE    4628 VERIFIED       4 HIT RXNS                      1 DOCS
SEARCH TIME: 00.00.02




     (FILE 'HOME' ENTERED AT 08:34:35 ON 12 MAR 2009)
                D SAVED

     FILE 'REGISTRY' ENTERED AT 08:35:06 ON 12 MAR 2009
                ACT SHA169REG/A
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L1             17 SEA SPE=ON  ABB=ON  (151052-40-3/BI OR 160514-13-6/BI OR
                   17100-68-4/BI OR 179089-03-3/BI OR 24856-58-4/BI OR 34421-94-8/
                   BI OR 61568-51-2/BI OR 676130-00-0/BI OR 676130-01-1/BI OR
                   676130-02-2/BI OR 676130-03-3/BI OR 676130-06-6/BI OR 862802-00
                   -4/BI OR 862802-02-6/BI OR 862802-03-7/BI OR 862802-04-8/BI OR
                   862802-05-9/BI)
                ---------
                D SCAN
                D SAVED
                ACT SHA169STR1/Q
                ---------
L2              STR
                ---------
                ACT SHA169STR2/Q
                ---------
L3              STR
                ---------
                D L2
                D L2
                D L3
L4              STR L3
L5             11 SEA SSS SAM L4
L6              STR L4
L7             50 SEA SSS SAM L6
L8          61787 SEA SSS FUL L6
                D L5
                D QUE L4
L9              STR L4
L10            19 SEA SUB=L8 SSS SAM L9
L11           300 SEA SUB=L8 SSS FUL L9
                SAVE TEMP L11 SHA169SUB1/A
L12             STR L2
```

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L13           0 SEA SUB=L8 SSS SAM L12
L14          16 SEA SPE=ON  ABB=ON  L1 AND L8
L15           3 SEA SPE=ON  ABB=ON  L1 AND L11
L16          13 SEA SPE=ON  ABB=ON  L14 NOT L15
                D QUE L12
L17          10 SEA SUB=L8 SSS FUL L12
                SAVE TEMP L17 SHA169SUB2/A
                D SCAN
                D STR RSD L17
L18      300689 SEA SPE=ON  ABB=ON  16.525/RID AND 46.150.18/RID
L19       56716 SEA SPE=ON  ABB=ON  L8 AND L18 NOT L17

     FILE 'CAPLUS' ENTERED AT 10:32:14 ON 12 MAR 2009
L20           7 SEA SPE=ON  ABB=ON  L17
L21           7 SEA SPE=ON  ABB=ON  L17/P
L22         902 SEA SPE=ON  ABB=ON  L11
L23       15869 SEA SPE=ON  ABB=ON  L19
L24           5 SEA SPE=ON  ABB=ON  L21 AND L22 AND L23
L25           7 SEA SPE=ON  ABB=ON  L21 AND (L22 OR L23)
L26           2 SEA SPE=ON  ABB=ON  L25 NOT L24
                D SCAN
                D SAVED
                ACT SHA169CAAU/A
                ---------
L27           1 SEA SPE=ON  ABB=ON  US2006-588169/AP
                ---------
L28          12 SEA SPE=ON  ABB=ON  KRELL C?/AU
L29         165 SEA SPE=ON  ABB=ON  HIRT H?/AU
L30           2 SEA SPE=ON  ABB=ON  (L27 OR L28 OR L29) AND (L20 OR L22 OR
                L23)

     FILE 'REGISTRY' ENTERED AT 10:35:40 ON 12 MAR 2009
L31        4594 SEA SPE=ON  ABB=ON  L8 AND CASREACT/LC

     FILE 'CASREACT' ENTERED AT 10:35:47 ON 12 MAR 2009
L32        3772 SEA SPE=ON  ABB=ON  L31
                D QUE NOS L17
                STR L12
L33           0 SEA SPE=ON  ABB=ON  US2006-588169/AP
L34           2 SEA SPE=ON  ABB=ON  KRELL C?/AU
L35           4 SEA SPE=ON  ABB=ON  HIRT H?/AU
L36           1 SEA SPE=ON  ABB=ON  L32 AND (L35 OR L36)
L37           0 SEA SUB=L32 SSS SAM L33 (     0 REACTIONS)
L38           0 SEA SSS SAM L33 (     0 REACTIONS)

     FILE 'REGISTRY' ENTERED AT 10:45:46 ON 12 MAR 2009

     FILE 'CASREACT' ENTERED AT 10:46:22 ON 12 MAR 2009
L39        3772 SEA SPE=ON  ABB=ON  L8
L40           1 SEA SPE=ON  ABB=ON  (L35 OR L36) AND L40
                D SCAN
L41           0 SEA SUB=L40 SSS SAM L33 (     0 REACTIONS)
                D QUE
L42           1 SEA SUB=L40 SSS FUL L33 (     4 REACTIONS)
                SAVE TEMP L43 SHA169CASRE/A
L43           1 SEA SPE=ON  ABB=ON  L41 AND L43

     FILE 'CAPLUS' ENTERED AT 10:49:07 ON 12 MAR 2009
                D QUE NOS L30
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     FILE 'CASREACT' ENTERED AT 10:49:07 ON 12 MAR 2009
                D QUE NOS L41

     FILE 'CASREACT, CAPLUS' ENTERED AT 10:49:14 ON 12 MAR 2009
L45             2 DUP REM L41 L30 (1 DUPLICATE REMOVED)
                      ANSWER '1' FROM FILE CASREACT
                      ANSWER '2' FROM FILE CAPLUS
                D IBIB ABS HIT 1
                D IBIB ABS HITSTR 2

     FILE 'CASREACT' ENTERED AT 10:49:56 ON 12 MAR 2009
                D STAT QUE L43
L46             0 SEA SPE=ON  ABB=ON  L43 NOT L41

     FILE 'REGISTRY' ENTERED AT 10:50:31 ON 12 MAR 2009
                D STAT QUE L11
                D STAT QUE L17
                D QUE NOS L19

     FILE 'CAPLUS' ENTERED AT 10:50:31 ON 12 MAR 2009
                D QUE NOS L25
L47             5 SEA SPE=ON  ABB=ON  L25 NOT L30
                D IBIB ABS HITSTR L47 1-5

     FILE 'HOME' ENTERED AT 10:50:48 ON 12 MAR 2009
                D STAT QUE L11
                D STAT QUE L17
                D STAT QUE L43

=>
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